UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/120,970	07/22/1998	ROY CURTISS III	53116-1763	2800

70953 7590 08/06/2007

LEON R. YANKWICH, ESQ.
YANKWICH & ASSOCIATES P.C.
201 BROADWAY
CAMBRIDGE, MA 02139

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
09120970	7/22/98	CURTISS ET AL.	53116-1763

LEON R. YANKWICH, ESQ.
YANKWICH & ASSOCIATES P.C.
201 BROADWAY
CAMBRIDGE, MA 02139

EXAMINER	
Ginny Portner	
ART UNIT	**PAPER**
1645	20070525

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

see attached Examiner's Answer

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/120,970
Filing Date: July 22, 1998
Appellent(s): CURTISS ET AL.

Mr. Leon R. Yankwich
Registration Number 30,237
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 14, 2006 appealing from the Office action mailed November 8, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is deficient. 37 CFR 41.37(c)(1)(v) requires the summary of claimed subject matter to include: (1) a concise explanation of the subject matter defined in each of the independent claims involved in the appeal, referring to the specification by page and line number, and to the drawing, if any, by reference characters and (2) for each independent claim involved in the appeal and for each dependent claim argued separately, every means plus function and step plus function as permitted by 35 U.S.C. 112, sixth paragraph, must be identified and the structure, material, or acts described in the specification as corresponding to each claimed function must be set forth with reference to the specification by page and line number, and to the drawing, if any, by reference characters. The brief is deficient because claimed invention is directed to a method of inducing an immune response in a warm-blooded animal and not to compositions of microbes. The method utilizes microbes that are bacteria that comprise an environmentally limited viability system and these bacteria are administered to an animal for induction of an immune response (claim 30).

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. Issue (1) is substantially correct. Issue (2) is correct. In issue (1) the changes are as follows: The obviousness type double patenting rejection was over the allowed

method of inducing immunoprotection in a vertebrate which administers a composition that comprises both a RADS and ELVS bacterial containment systems based upon the methods step of administering the bacteria containing an environmentally trans-regulatory element (araCP.sub.BAD, allowed claims 1, 5, 7, 10 and 12) to a vertebrate to induce an immune response, specifically immunoprotection to an administered antigen, see allowed methods claim 24 in US Patent 6,780,405. The allowed species anticipates the instantly claimed genus.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 61-64 are rejected under 35 U.S.C. 112, first paragraph as failing to provide an enabling disclosure.

It is apparent that the claimed extrachromosomal vector comprising pMEG-104 is required to practice the claimed invention. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the plasmid vector, see 37 C.F.R. 1.802.

The necessary criteria of the deposit rules under the terms of the Budapest Treaty must be met. An affidavit or declaration by Appellants, or a statement by an attorney of record stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions

imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.801-37 CFR 1.809.

2. Claim 30, 32-33,35-38, 39, 50-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24 and claims 1-23 (claim 20 defined to include Salmonella) of U.S. Patent No. **6,780,405**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed species of method of inducing an immunoprotective immune response in a vertebrate anticipates the instantly claimed invention of inducing any type of immune response in an animal, wherein the composition administered in the instant Application comprises a bacteria that may or may not be attenuated, but the allowed species of microorganism must be attenuated (see'405, claim 19), the viability system of the instant Application may be controlled by any number or regulateable control sequences, but the allowed method administers a species which requires specific regulatory sequences (see claims 1-18).

(10) Response to Argument

3. Appellant's arguments filed June 10, 2005 have been fully considered but they are not persuasive.

4. Appellant asserts that:

a. "The object of the '405 patent is to design a system that produces and releases large amounts of antigen at a desired time, e.g. after inoculation. It is not seen how this RAV system can be considered an obvious variant of an ELV system designed for

biological containment, ie, to prevent the vaccine microorganism from surviving in selected non-permissive environments.

5. It is the position of the examiner that the method comprising the step of "administering the vaccine " administers a microorganisms (encompasses Salmonella bacteria) that comprises both a RAV and ELV system in the allowed method of inducing immunoprotection in a vertebrate (allowed claim 24), thus administering a species encompassed by the instantly claims genus of methods that administer a bacterium that comprises an ELV system.

6. The compositions of '405 are defined by the allowed claims and the definitions provided by the Specification of '405. Claim 7 of '405 is directed to a microorganism which comprises an environmentally regulatable control sequence, specifically araCPbad, which is activate able by arabinose AraCPbad is regulatable control sequence disclosed to function as a trans regulatory element. A portion of the '405 Specification is quoted immediately below to show one of the definitions of the AraCPbad regulatory control sequence:

- "Depending on the turnover of the trans regulatory element and the relationship between the amount of trans regulatory element on hand and the amount of trans regulatory element needed to maintain the low copy number regime, the low copy number regime can be maintained for several generations after transfer to the high copy number environment. Such temporary low copy number condition can be useful, for example, for allowing the host microorganism to colonize the host in a high copy number environment (e.g., without arabinose), such as an animal, but not remain indefinitely. As such, the RADS is a *containment system* even without the phage lysis genes described in WO96/40947. A delayed RADS is also useful when the desired gene product is harmful to the host cell, as in Example 3. Additionally, the delayed RADS can be used to

depend an essential gene of a balanced lethal host system, such as asd, on an activateable control sequence such as araCP.sub.BAD, to provide for a weakening of the cell wall upon immunization (and withdrawal of, in this case, arabinose). See Example 5."

Additionally, the Specification of '405 defines the RAV and RAD system to also comprise an ELV system; this preferred embodiment comprising the araCPbad environmentally regulatable control sequence. Quoting the Specification :

- "A preferred method for causing this lysis is an ELVS system, as described in WO96/40947. In that system, vector-borne lethal genes such as the phage lysis genes lys 13 and lys 19 are operably linked to P22 P.sub.R and the chromosome-encoded C2 repressor is operably linked to **araCP.sub.BAD**. Introduction of the strain into an environment without arabinose, such as in an inoculated animal, results in a dilution of the C2 repressor present until the lethal gene products kill the cell. In addition, the RADS with a RAV comprising a transfer vector can be designed as an **ELVS** that lysis due to regulated lysis genes inserted into the chromosome. Such expression of lysis genes would exhibit delayed expression such that lysis would only occur after the vertebrate cells with the transfer vector had entered a eukaryotic cell and conferred runaway vector replication. See also Example 6, which describes novel transfer vector adaptations to the RADS. When properly designed, the ELVS system is fully compatible with the RADS system and may share control elements. In this case, lysis of the cell, for example caused by an ELVS, will release the transfer vector inside the recipient cell. For expression of genes on the transfer vector in recipient cells, it is preferred that the expression genes be operatively linked to expression control sequences operable in the recipient cell. For example, where the recipient cell is an animal cell, it

is preferred that the expression genes be operatively linked to a promoter functional in the animal and possess sequences ensuring polyadenylation of the mRNA. Methods for engineering such sequences are well known in the art." (emphasis added)

- The microorganism of allowed claim 7 of '405 is defined to comprise not only the RAD/RAV system, but also to comprise the ELVS system and is administered in the method of allowed claim 24. Therefore, the allowed claim 24 of '405 is directed to a species which utilizes a specific environmentally regulatable control sequence, specifically araCPbad. The allowed species anticipates the instantly claimed genus of method now claimed. Additional claims were added to the ODP rejection in light of the amendment of claim 65 to depend from claim 65, and the specific definitions of the allowed species of regulatable control sequence provided by '405 to be in trans relationship to an essential asd gene, and lysis genes from bacteriophage P22. The obviousness type double patenting rejection is herein maintained.

7. Appellant provided a correspondence table traversing the obviousness type double patenting rejection.

8. In response the examiner stated in the Advisory action dated June 1, 2006 , the correspondence table compared the instant method with a composition claim, rather than the method claim of the issued patent utilized in the obviousness type double patenting rejection made of record. The examiner provided a correspondence table over the claims.

Correspondence table between the instant Application claims 09/120,970 (claims 30, 32-33, 35-60 and 65) and allowed methods claim 24, in light of the compositions defined in claims 1-23 of US Pat. 6,780,405.

The disclosure of 6,780,405 is utilized for definitions of the claimed method, the method administering the allowed compositions defined therein.

The environmentally regulateable control sequence is a coding sequence effected by environmental arabinose.

09/120,970	**6,780,405**
* **method claim** 30	*claim 24 (dep. From clm 1,5,19)
* **inducing immune response**	***inducing immunoprotection (species of immune response)**
***administering**	* **administering**
* **attenuated bacterial cell/**(instant claim 30, 36, 37) **expression gene**	* **inactivated Salmonella** (clm. 6, 8) **encodes desired gene product**
***antigen introduced into the animal**	***antigen admin. (introduced) to vertebrate**
***containment system (viable in animal/nonviable outside)**	***RADS is a species of containment system**

'405 at col. 23, lines 21-38 and col. 24, lines 32-35 defines the RADS to comprise ELVS components and '405, allowed claims 21-22 are so defined:

- "In that system, vector-borne lethal genes such as the phage lysis genes lys 13 and lys 19 are operably linked to P22 P.sub.R and the chromosome-encoded C2 repressor is operably linked to **araCP.sub.BAD** (claimed in '405, allowed claims 7, 10, 12 which depend from claim 5). Introduction of the strain into an environment without arabinose, such as in an inoculated animal,

results in a dilution of the C2 repressor present until the lethyl gene products kill the cell. In addition, the RADS with a RAV comprising a transfer vector can be designed as an ELVS that lysis due to regulated lysis genes inserted into the chromosome. Such expression of lysis genes would exhibit delayed expression such that lysis would only occur after the vertebrate cells with the transfer vector had entered a eukaryotic cell and conferred runaway vector replication. See also Example 6, which describes novel transfer vector adaptations to the RADS. When properly designed, the ELVS system is fully compatible with the RADS system and may share control elements. In this case, lysis of the cell, for example caused by an ELVS, will release the transfer vector inside the recipient cell."

Additionally, the '405 Specification definitions set forth the AraCPbad regulatory control sequence to be an integral component of a RADS containment system, this regulatory control being claimed in '405 allowed (claims 5-7 and 21- 22).

- "Depending on the turnover of the trans regulatory element and the relationship between the amount of trans regulatory element on hand and the amount of trans regulatory element needed to maintain the low copy number regime, the low copy number regime can be maintained for several generations after transfer to the high copy number environment. Such temporary low copy number condition can be useful, for example, for allowing the host microorganism to colonize the host in a high copy number environment (e.g., without arabinose), such as an animal, but not remain indefinitely. As such, the *RADS is a containment system* even without the phage lysis genes described in WO96/40947. A delayed RADS is also useful when the desired gene product is harmful to the host cell, as in Example 3. Additionally, the delayed RADS can be used to depend *an essential gene of a balanced lethal host system*, such as asd, on an activateable control sequence such as araCP.sub.BAD, to provide for a weakening of the cell wall upon immunization (and withdrawal of, in this case, arabinose). See Example 5." The "araCPsubBAD" control sequence is claimed in

'405 claim 7 which depends from claim 5, form which the method claim 24 indirectly depends.

Clm 32: antigen sources	claim 24 : antigen, defined to be a vaccine antigen Col. 31, lines 30-35
Clm 33: mucosal	claim 24: admin. MALT (mucosal: column 13,lines 24-29;col. 31,lines 24-25)
Clm. 35: replication gene	"a second ori conferring vector replication " Allowed claim 1.
Clm. 38: GALT or BALT	claim 24: admin. GALT or BALT ('405, col.13, lines 14-19)
Clm 39: lethal gene	claim 24: "lethyl gene product kills the cell",col. 23,lines 25-26
Clm. 40-43: cell wall essential gene	Clm. 24: balanced lethal system, asd gene is an essential gene for cell wall biosynthesis (see examples and col. 23-24).
Clm. 45-46: P22 lysis genes 13 & 19	Clm 24: defined microorganism to include the P22 lysis genes, 13 & 19; also see allowed claims 18-23; col. 23, lines 21-38 and col. 24, lines 32-35 defines the RADS to comprise ELVS, the lysis genes being integrated into the bacterial chromosome and are not located on the plasmid runaway vector.

- Therefore, the corresponding support for each of the recited claim limitations shows the allowed method claim 24 of '405 to be defined as a species within the claimed genus of methods of the instant Application.
- The allowed species still anticipates the instantly claimed genus of methods.
- The obviousness type double patenting could be obviated by submission of an effective terminal disclaimer.

9. The compositions of '405 are defined by the allowed claims and the definitions provided by the Specification disclosure of '405. Claim 7 of '405 is directed to a microorganism which comprises an environmentally regulatable control sequence, specifically araCPbad, which is activate able by arabinose AraCPbad regulatable control sequence is disclosed to function as a trans regulatory element. A portion of the '405 Specification is quoted immediately below to show one of the definitions of the AraCPbad regulatory control sequence:

- "Depending on the turnover of the trans regulatory element and the relationship between the amount of trans regulatory element on hand and the amount of trans regulatory element needed to maintain the low copy number regime, the low copy number regime can be maintained for several generations after transfer to the high copy number environment. Such temporary low copy number condition can be useful, for example, for allowing the host microorganism to colonize the host in a high copy number environment (e.g., without arabinose), such as an animal, but not remain indefinitely. As such, the RADS is *a containment system* even without the phage lysis genes described in WO96/40947. A delayed RADS is also useful when the desired gene product is harmful to the host cell, as in Example 3. Additionally, the delayed RADS can be used to depend an essential gene of a balanced lethal host system, such as asd, on an activateable control sequence such as araCP.sub.BAD, to provide for a weakening of the cell wall upon immunization (and withdrawal of, in this case, arabinose). See Example 5."

Additionally, the Specification of '405 defines the RAV and RAD system to also comprise an ELV system; this preferred embodiment comprising the araCPbad environmentally regulatable control sequence. Quoting the Specification :

- "A preferred method for causing this lysis is an ELVS system, as described in WO96/40947. In that system, vector-borne lethal genes such as the phage lysis genes lys 13 and lys 19 are operably linked to P22 P.sub.R and the chromosome-encoded C2 repressor is operably linked to **araCP.sub.BAD**. Introduction of the strain into an environment without arabinose, such as in an inoculated animal, results in a dilution of the C2 repressor present until the lethal gene products kill the cell. In addition, the RADS with a RAV comprising a transfer vector can be designed as an **ELVS** that lysis due to regulated lysis genes inserted into the chromosome. Such expression of lysis genes would exhibit delayed expression such that lysis would only occur after the vertebrate cells with the transfer vector had entered a eukaryotic cell and conferred runaway vector replication. See also Example 6, which describes novel transfer vector adaptations to the RADS. When properly designed, the ELVS system is fully compatible with the RADS system and may share control elements. In this case, lysis of the cell, for example caused by an ELVS, will release the transfer vector inside the recipient cell. For expression of genes on the transfer vector in recipient cells, it is preferred that the expression genes be operatively linked to expression control sequences operable in the recipient cell. For example, where the recipient cell is an animal cell, it is preferred that the expression genes be operatively linked to a promoter functional in the animal and possess sequences ensuring polyadenylation of the mRNA. Methods for engineering such sequences are well known in the art." (emphasis added)

- The microorganism of allowed claim 7 of '405 is defined to comprise not only the RAD/RAV system, but also to comprise the ELVS system and is administered in the method of allowed claim 24. Therefore, the allowed claim 24 of '405 is directed to a species which

utilizes a specific environmentally regulatable control sequence, specifically araCPbad. The allowed species anticipates the instantly claimed genus of method now claimed. Additional claims were added to the ODP rejection in light of the amendment of claim 65 to depend from claim 65, and the specific definitions of the allowed species of regulatable control sequence provided by '405 to be in trans relationship to an essential asd gene, and lysis genes from bacteriophage P22. The obviousness type double patenting rejection is herein maintained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Ginny Portner
Patent Examiner
Art Unit 1645

Conferees:

Jeff Siew

Supervisory Patent Examiner

Art Unit 1645

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

Mark Navarro

Primary Examiner

Art Unit 1645